

### **REMARKS**

The Official action mailed 9 November 2007, has been received and its contents carefully noted. Claims 1-5, 11-17, 20-24 and 36 were rejected and claims 6-10 and 18-19 were withdrawn from consideration. By this amendment, claims 1-36 have been canceled and claims 37-46 have been added. Support may be found in the specification and the claims as originally filed. No statutory new matter has been added. Therefore, reconsideration and entry of the claims as amended are respectfully requested.

#### **Rejection under 35 U.S.C. 112, second paragraph**

The Examiner rejected claims 1-5, 11-17, 20-24 and 36 under 35 U.S.C. 112, second paragraph, as being indefinite for containing the term "modulating". The Examiner also rejected claims 1-5, 2, 21, 24 and 36 for containing an abbreviation "PKC", claim 2 for containing the term "derivative", and claim 20 for lacking antecedent basis.

Applicants direct the Examiner's attention to the definition of a rottlerin "derivative" provided in the specification as originally filed on page 43, paragraph 171. In view of this definition, Applicants respectfully urge that the scope and meaning of "derivative" in claim 2 is clear and definite.

Applicants respectfully submit that the claims, as amended, overcome the remaining rejections under 35 U.S.C. 112, second paragraph.

Therefore, Applicants respectfully assert that the claims, as amended, are clear and definite and the rejection under 35 U.S.C. 112, second paragraph, should properly be withdrawn.

#### **Rejection under 35 U.S.C. 112, first paragraph**

The Examiner rejected claims 1-5, 11-17, 20-24 and 36 under 35 U.S.C. 112, first paragraph, as lacking enabling support for "preventing" pancreatic cancer or pancreatitis.

Applicants respectfully submit that the claims, as amended, are not directed to "preventing" cancer and pancreatitis.

Therefore, Applicants respectfully urge that the claims, as amended, are enabled and the rejection under 35 U.S.C. 112, first paragraph, should properly be withdrawn.

### **Rejection under 35 U.S.C. 102(b)**

The Examiner rejected claims 1-5, 11-17, 20-24 and 36 under 35 U.S.C. 102(b) as being anticipated by Agus et al. (2000) Carcinogenesis 21(6):1213-1219. Specifically, the Examiner stated that Agus et al. discloses that rottlerin and genistein inhibits binding of a carcinogen to DNA. The Examiner then stated that although apoptosis or inhibition of nucleic acid synthesis by rottlerin and capsase activation by are not taught by Agus et al., both are inherent given that they are commonly known to occur during administration of an agent aiding in the treatment of cancer or inflammation.

Applicants respectfully submit that Agus et al. does not teach that cancer and inflammation can be treated by administering rottlerin or a derivative thereof. Specifically, Agus et al. merely discloses that genistein and rottlerin inhibits a compound from binding DNA. The compound, 2-amino-3-methylimidazo[4,5-f]quinoline, is known to be a carcinogen. Agus et al., however, does not teach that cancer is definitively caused when this compound binds DNA. In other words, Agus et al. does not rule out the possibility that 2-amino-3-methylimidazo[4,5-f]quinoline is involved in another mechanism which consequently causes cancer. Hence, nowhere does Agus et al. teach or suggest that rottlerin or a derivative thereof inhibits cancer or inflammation. Again, Agus et al. only discloses that rottlerin and genistein inhibit the binding of 2-amino-3-methylimidazo[4,5-f]quinoline to DNA. In addition, nowhere does Agus et al. teach or suggest that rottlerin or a derivative thereof treats or inhibits *pancreatic* cancer or *pancreatitis*.

Therefore, Agus et al. does not teach or suggest the claimed invention and the rejection under 35 U.S.C. 102(b) should properly be withdrawn.

### **Rejection under 35 U.S.C. 103(a)**

The Examiner rejected claims 1-5, 11-17, 20-24 and 36 under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (US 20040023925) in view of Glimcher et al. (US 20050026285). Specifically, the Examiner deemed that it would have been obvious to administer genistein and rottlerin to prevent or inhibit NF-kB activation since the Examiner deemed that both are directed to treating cancer.

Applicants respectfully submit that the present invention, as claimed, is directed to treating or inhibiting pancreatic cancer or pancreatitis by administering rottlerin or a derivative

thereof. Chang et al. is directed to enhancing the efficacy of chemotherapy by co-jointly administering a compound which binds to a galectin. Chang et al. does not disclose anything having to do with administering rottlerin or a derivative thereof.

Glimcher et al., does not alleviate the deficiencies of Chang et al. Glimcher et al. merely discloses that rottlerin blocks KRC transactivation of the AP-1 reporter (§¶0117) and uses rottlerin in an experiment showing that KRC does not modulate MAPK activity (§¶0123, ¶0444, ¶0455). Glimcher et al. does not disclose anything having to do with pancreatic cancer or pancreatitis.

Thus, Applicants respectfully submit that one of ordinary skill in the art would not have been motivated to combine the disclosures of Chang et al. and Glimcher et al. to result in a method of treating pancreatic cancer or pancreatitis using rottlerin or a derivative thereof with a reasonable likelihood of success. In fact, Applicants respectfully submit that since Glimcher et al. only discloses that rottlerin blocks KRC transactivation of the AP-1 reporter, the combination of Chang et al. and Glimcher et al. does not result in the claimed invention as a whole – administering rottlerin or a derivative thereof to treat or inhibit pancreatic cancer or pancreatitis.

Applicants note that the prior art discloses that rottlerin may be effective against a few specific types of cancers such as colon cancer and some malignant gliomas. See e.g. Tillman et al. (2003) Cancer Res. 63(16):5118-5125, and Parmer et al. (1997) Cell Grow. Differ. 8(3):327-334. Prior to the present invention, however, it was unknown that rottlerin would be effective against pancreatic cancer or pancreatitis. Those skilled in the art are well aware that a given compound may be effective against a given disease in a given tissue and that the same compound may not be effective against a similar disease in a different tissue. In fact, it is well known to those skilled in the art that a given chemotherapeutic may be effective against a given cancer, but not against another cancer. In fact, the review by McKenna & Eatock demonstrate that certain chemotherapies, such as taxanes, have limited activity against pancreatic cancer. See McKenna & Eatock (2003) The Oncologist 8:149-160.

Thus, just because rottlerin may be effective against a cancer, such as colon cancer, one of ordinary skill in the art would not administer rottlerin or a derivative thereof with a reasonable expectation of successfully treating or inhibiting pancreatic cancer or pancreatitis. Prior to the present invention, rottlerin was known to have a differential effect in various biochemical pathways linked to inflammation and various cancers. Specifically, Vancurova et al. disclosed

that rottlerin does not inhibit LPS and IL-1 $\beta$  NF-kB activation. See Vancurova et al. (2001) JBC Papers in Press, page 13. In fact, although the various scientific journal articles cited below have publication dates after the effective filing date of the present invention, the articles prove that rottlerin is not effective against some cancers such as lymphoma, thyroid cancer, leukemia, and breast cancer. Specifically,

Nakajima et al. (2006) Mutation Research 595:29-36 teaches that rottlerin “completely abolished radiation-induced apoptosis” in a lymphoma cell line.

Koike et al. (2006) Thyroid 16(4):333-341 teaches that rottlerin reverses the cycle arrest cause by phorbol 12-myristate 13-acetate in thyroid cancer cells.

Yan et al. (2007) Leukemia 21:1488-1495 teaches that rottlerin “markedly decreased bortezomib plus ATO-induced apoptosis” in leukemic cells. Bortezomib and ATO (arsenic trioxide) are chemotherapeutic agents.

Kaur et al. (2005) Exper. Hematology 33:550-557 teaches that rottlerin reverses the anti-leukemic effects of interferon-alpha. See the last sentence before the Discussion on page 554 and Figure 5.

Yokoyama et al. (2005) Biochem. Biophys. Res. Comm. (2005) 327:720-726 teaches that rottlerin reverses the inhibitory effect of phorbol 12-myristate 13-acetate on cell proliferation in breast cancer. See Figure 3 on page 723 and the paragraph above this figure describing it.

Lee et al. (2007) J. Biol. Sciences 282(20):15271-15283 teaches that rottlerin reverses apoptosis caused by sanguinamycin in breast cancer cells.

Thus, Applicants respectfully submit that one skilled in the art would not have been motivated to administer rottlerin or a derivative thereof with a reasonable likelihood of successfully treating or inhibiting pancreatic cancer or pancreatitis.

Therefore, the claimed invention is unobvious and the rejection under 35 U.S.C. 103(a) should properly be withdrawn.

#### **Request for Interview**

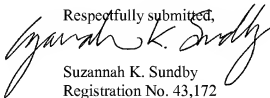
Either a telephonic or an in-person interview is respectfully requested should there be any remaining issues.

### CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Therefore, it is respectfully requested that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Official action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. 1.136(a), and any fees required therefor are hereby authorized to be charged to **Deposit Account No. 02-4300**, Attorney Docket No. **034044.021CIP1**.

Respectfully submitted,



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